US011984310B2

(12) **United States Patent**
Lehmann et al.

(10) **Patent No.: US 11,984,310 B2**
(45) **Date of Patent: May 14, 2024**

(54) **MASS SPECTROMETRY APPARATUS**

(71) Applicant: **Analytik Jena GmbH**, Jena (DE)

(72) Inventors: **Roland Lehmann**, Jena (DE); **Wolfram Weisheit**, Saara (DE); **Iouri Kalinitchenko**, Jena-Maua (DE)

(73) Assignee: **Analytik Jena GmbH**, Jena (DE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 78 days.

(21) Appl. No.: **17/663,074**

(22) Filed: **May 12, 2022**

(65) **Prior Publication Data**

US 2022/0367167 A1 Nov. 17, 2022

(30) **Foreign Application Priority Data**

May 12, 2021 (EP) 21173703

(51) **Int. Cl.**
H01J 49/10 (2006.01)
H01J 49/00 (2006.01)
H01J 49/04 (2006.01)
H01J 49/06 (2006.01)

(52) **U.S. Cl.**
CPC ***H01J 49/105*** (2013.01); ***H01J 49/0031*** (2013.01); ***H01J 49/0495*** (2013.01); ***H01J 49/067*** (2013.01)

(58) **Field of Classification Search**
CPC .. H01J 49/105; H01J 49/0031; H01J 49/0495; H01J 49/067; H01J 49/14; H01J 49/0422; H01J 49/26
USPC 250/282
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,948,962	A *	8/1990	Mitsui	H01J 49/12 250/281
5,559,337	A	9/1996	Ito	
5,773,823	A	6/1998	Ito	
5,804,821	A	9/1998	Nakagawa	
6,031,579	A	2/2000	Stephenson	
6,265,717	B1 *	7/2001	Sakata	H01J 49/067 250/281
6,614,021	B1	9/2003	Kalinitchenko	
6,630,665	B2	10/2003	Tanner et al.	

(Continued)

FOREIGN PATENT DOCUMENTS

DE	202020106423	U1	2/2021
WO	2004012223	A1	2/2004

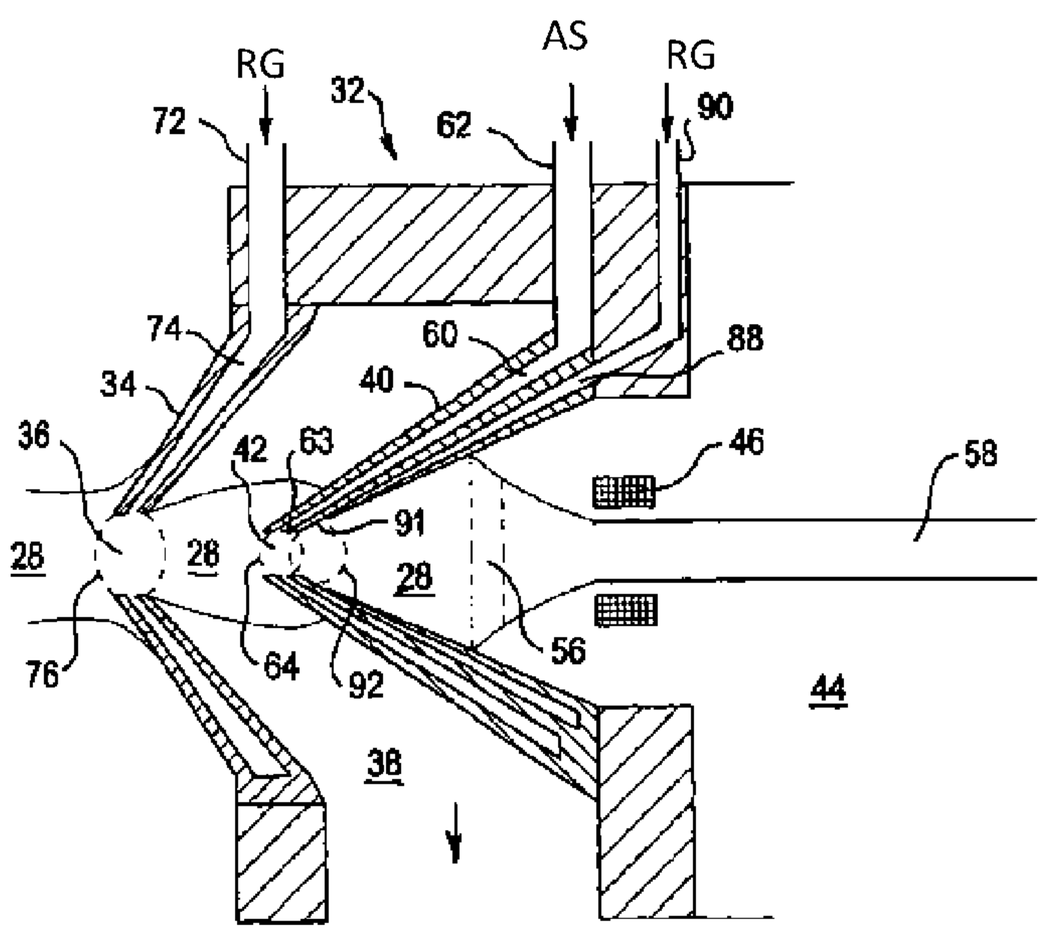
(Continued)

Primary Examiner — Kiet T Nguyen
(74) *Attorney, Agent, or Firm* — Christopher R. Powers; Endress+Hauser (USA) Holding, Inc.

(57) **ABSTRACT**

A method of operating an inductively coupled plasma mass spectrometry apparatus for analyzing an analyte sample, the mass spectrometry apparatus including a plasma ion source, a mass analyzer and an interface arrangement positioned between the plasma ion source and the mass analyzer of the mass spectrometer, the interface arrangement at least including an interface structure, including a sampling or skimmer cone, and at least one passage with an inlet and an outlet into a reaction zone, the method including: generating a plasma using the plasma ion source and forming a plasma flux to flow towards the mass analyzer; supplying the analyte sample into the reaction zone via the passage such that the analyte sample interacts with the plasma flux; and analyzing the analyte sample using the mass analyzer.

15 Claims, 3 Drawing Sheets



(56) **References Cited**

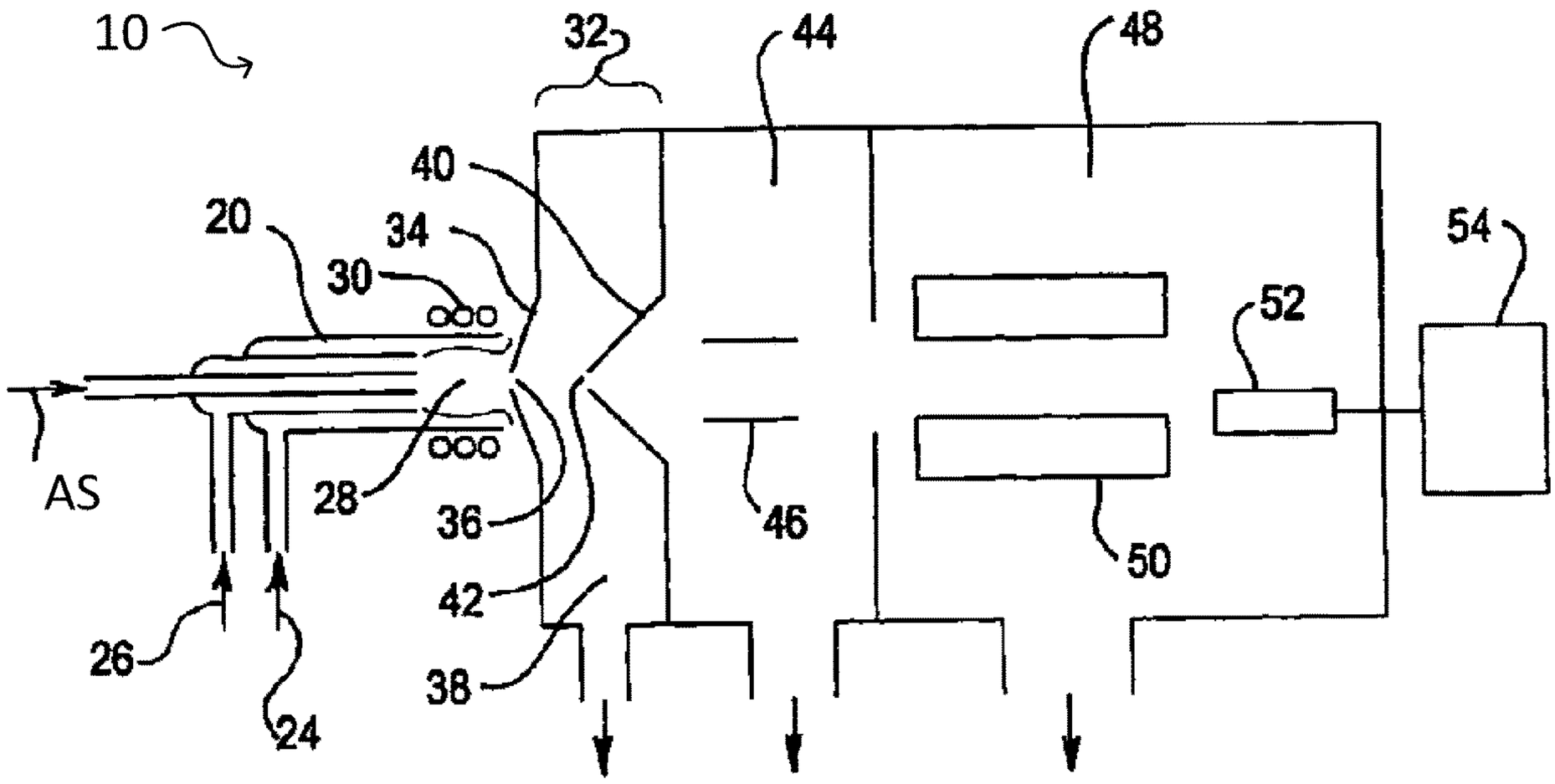
U.S. PATENT DOCUMENTS

6,815,667	B2	11/2004	Tanner et al.
7,119,330	B2	10/2006	Kalinitchenko
7,329,863	B2	2/2008	Kalinitchenko
2016/0026747	A1	1/2016	Garaas et al.
2018/0240662	A1	8/2018	Schwieters et al.

FOREIGN PATENT DOCUMENTS

WO	2012024570	A2	2/2012
WO	2016096457		6/2016
WO	2017176131	A1	10/2017

* cited by examiner



PRIOR ART

Fig. 1

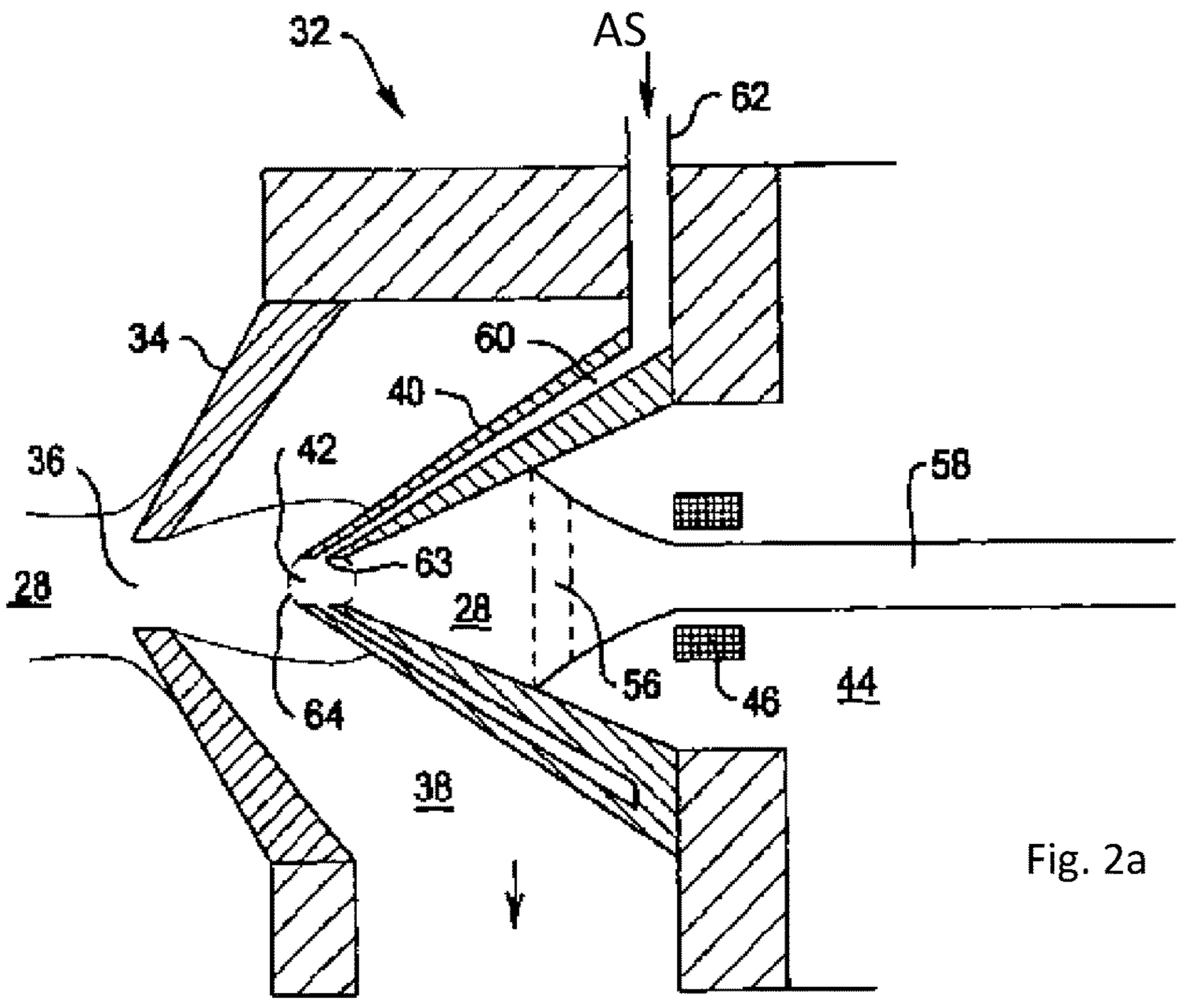


Fig. 2a

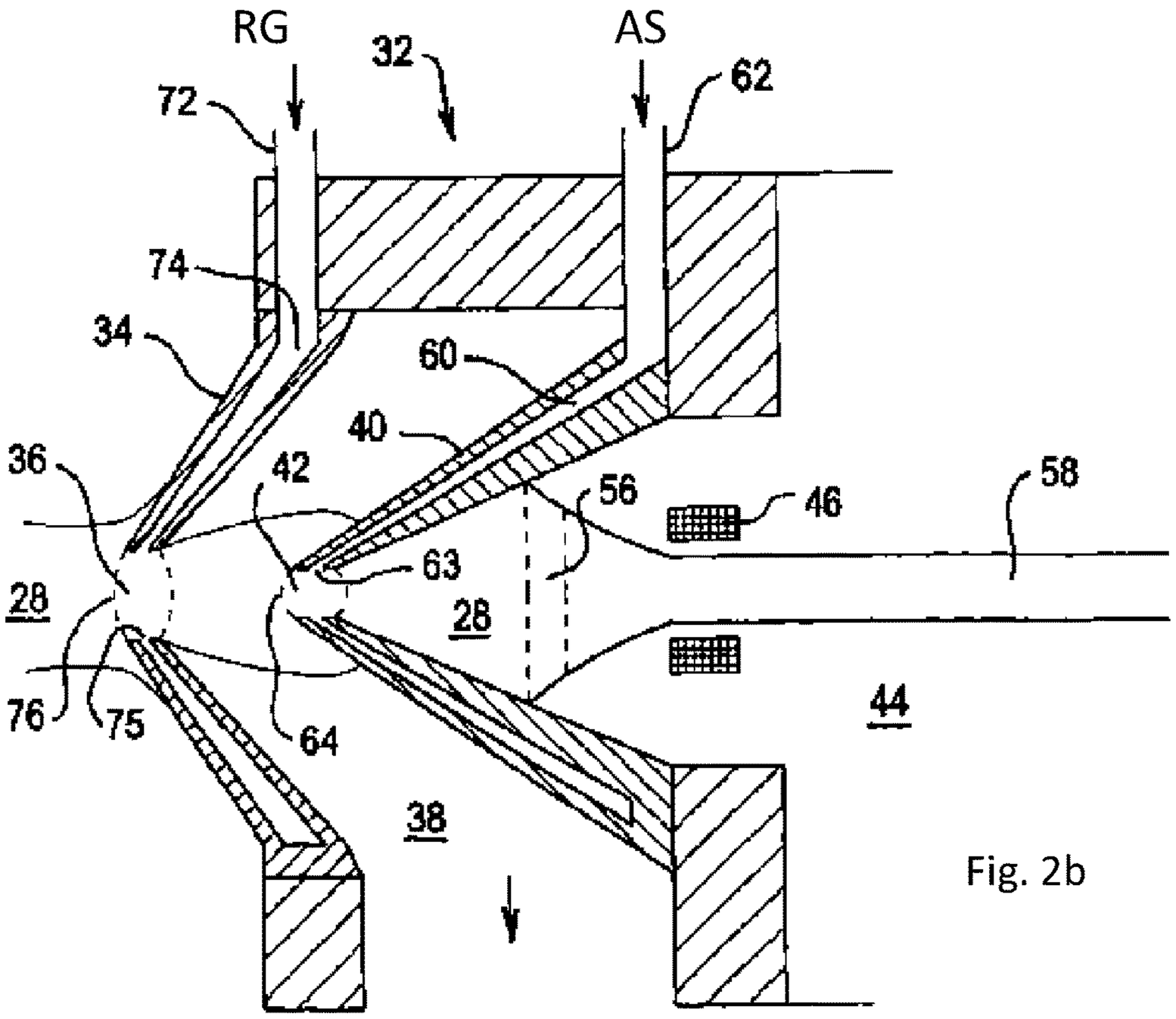

RG
AS
32
72
62
74
34
60
40
36
42
56
46
58
63
28
28
76
75
64
44
38

Fig. 2b

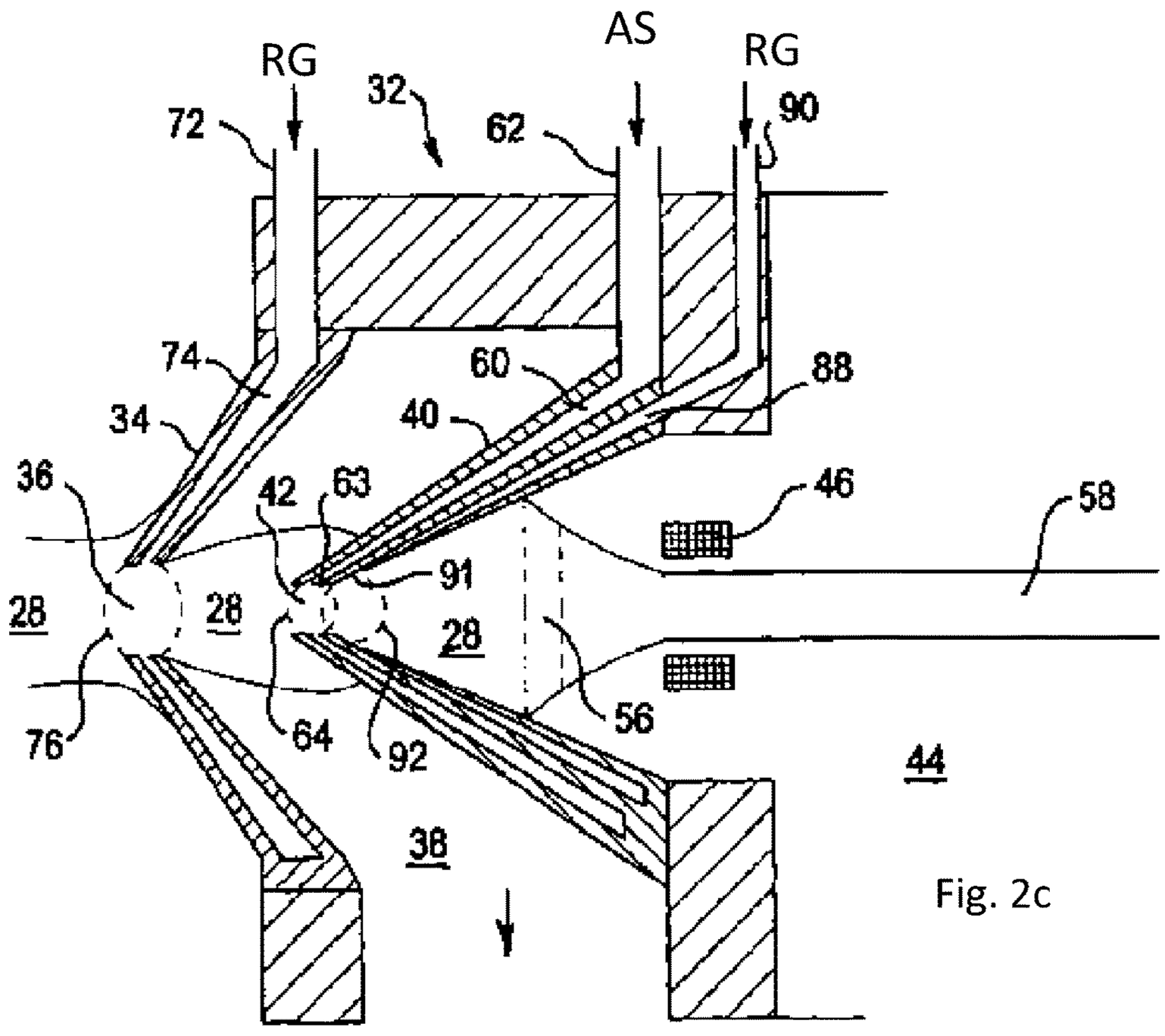

RG
AS
RG
32
72
62
90
74
60
88
34
40
36
42
63
46
58
91
28
28
28
76
64
92
56
44
38

Fig. 2c

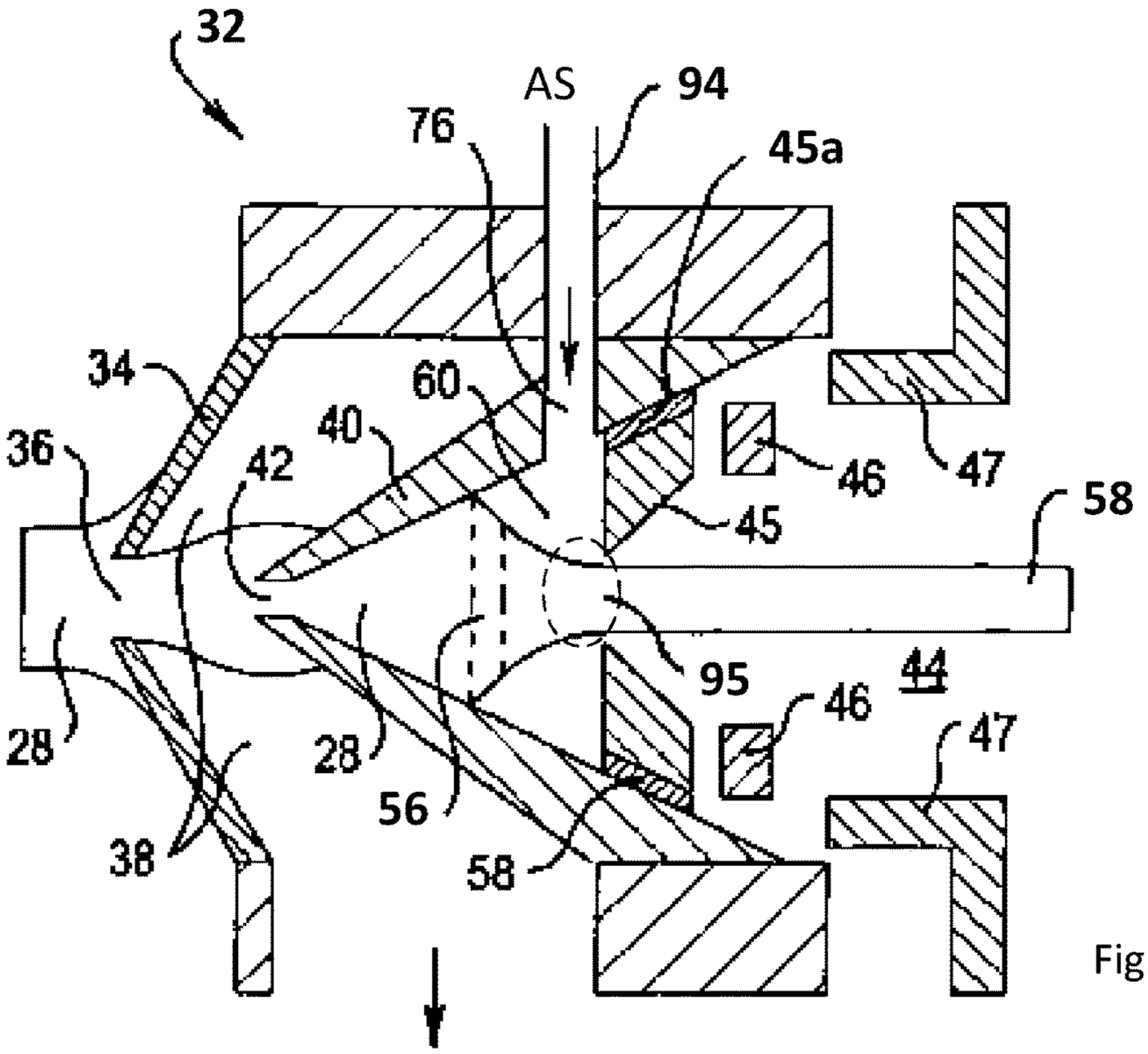

32
AS
94
76
45a
34
60
40
36
42
46
47
45
58
95
44
28
28
46
47
56
38
58

Fig. 2d

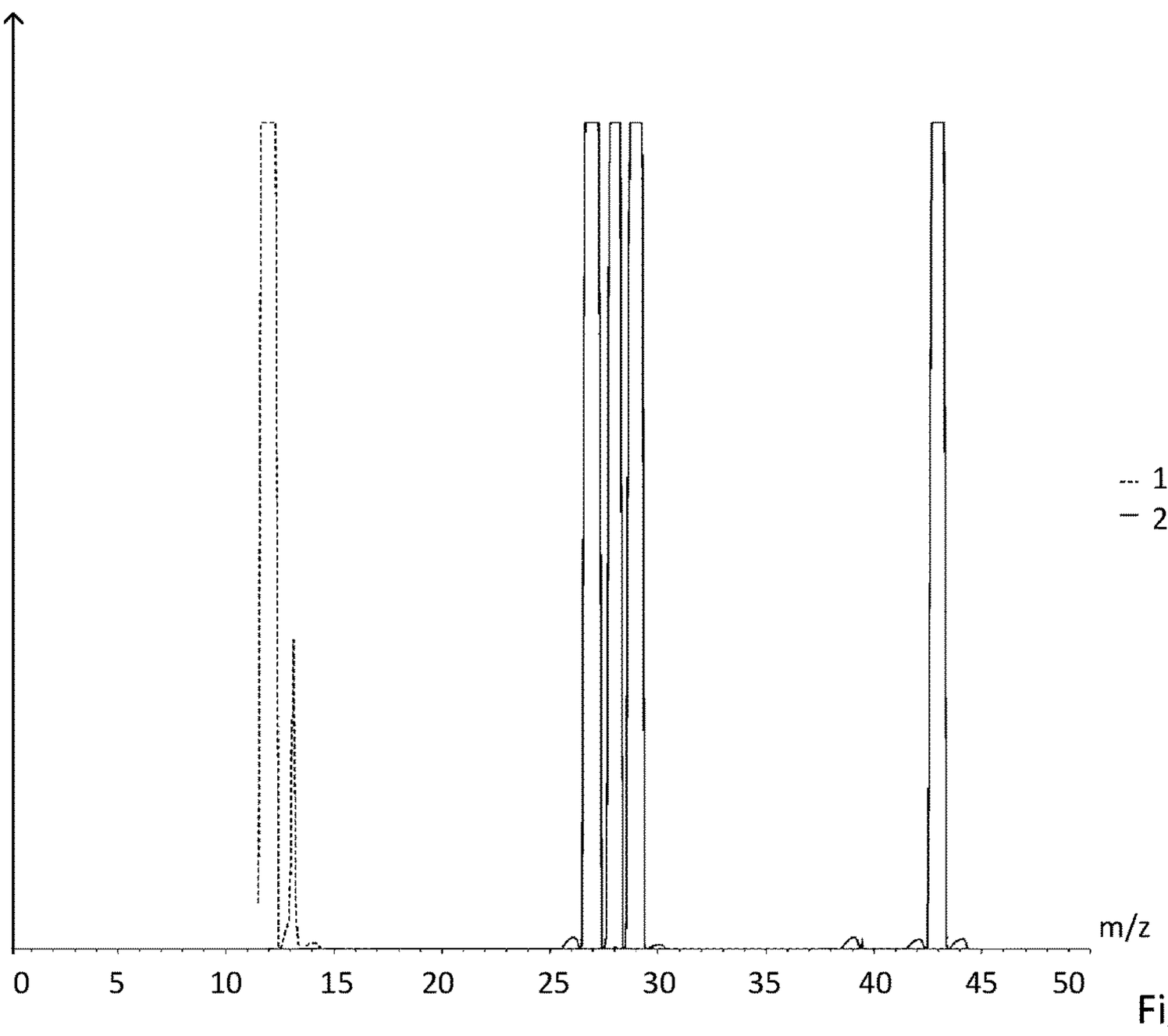

1
2
m/z
0
5
10
15
20
25
30
35
40
45
50

Fig. 3

MASS SPECTROMETRY APPARATUS

CROSS-REFERENCE TO RELATED APPLICATION

The present application is related to and claims the priority benefit of European Patent Application No. 21173703.6, filed May 12, 2021, the entire contents of which are incorporated herein by reference.

TECHNICAL FIELD

The present disclosure relates to a method of operating an inductively coupled plasma mass spectrometry apparatus for analyzing a molecular analyte substance or a mixture of at least two substances.

BACKGROUND

Inductively coupled plasma mass spectrometers (ICP-MS) are, e.g., used for trace element analysis. Typically, an ICP-MS analysis involves the complete atomization and subsequent ionization of the test sample by means of a plasma source before the resulting elemental ions are quantified by the spectrometer. Up to now, several different types of ICP-MS are available, such as, e.g., the quadrupole ICP-MS or time-of-flight ICP-MS.

A common problem of any ICP-MS analysis is the possible occurrence of interferences caused by newly forming polyatomic ions or molecules. Such interferences are often addressed by means of reaction/collision cells in the respective ICP-MS system, whereby reagent gases are added to the reaction/collision cell to provide for a separation of analyte ions from interferences based upon their energy differences. An exemplary ICP-MS system for improved attenuation of interferences is described in U.S. Pat. No. 7,329,863 B2 and U.S. Pat. No. 7,119,330 B2.

ICP-MS systems are less suitable or even unsuitable for the analysis of molecules, which are typically investigated by mass spectrometers employing different types of ionization sources, e.g., electrospray-ionization (ESI) or atmospheric pressure chemical ionization (APCI). Such methods are optimized for the ionization of molecules and do not lead to an atomization of them.

Other mass spectrometry systems suitable for molecular analysis are, e.g., the selected-ion flow-tube mass spectrometer (SIFT-MS) or the proton-transfer-reaction mass spectrometer (PTR-MS)

However, up to now, no mass spectrometry system is available, which allows for the analysis of atomized and ionized molecules in one single device.

SUMMARY

Therefore, the objective technical problem underlying the present disclosure is to provide such possibility for analyzing atomized and ionized molecules in one single device. This object is achieved by the method and by the use according to the present disclosure.

Regarding the method, the object is achieved by a method of operating an inductively coupled plasma mass spectrometry apparatus for analyzing an analyte sample, the mass spectrometry apparatus including a plasma ion source, a mass analyzer and an interface arrangement positioned between the plasma ion source and the mass analyzer of the mass spectrometer, the interface arrangement at least comprising an interface structure in the form of a cone, e.g., a sampling cone or a skimmer cone, and at least one passage with an inlet and an outlet, the passage leading from an outside of the interface structure into a reaction zone formed in an area surrounding the outlet of the passage.

The method comprises the steps of: generating a plasma using the plasma ion source and forming a plasma flux to flow towards the mass analyzer; supplying the analyte sample into the reaction zone via the passage such that the analyte sample interacts with the plasma flux; and analyzing the analyte sample using the mass analyzer.

The molecular analyte substance or mixture may initially be provided in the form of a gas, a vapor or a liquid. The analyte sample preferably is a molecular analyte substance or a mixture of at least two substances.

The interface structure may comprise one or more cones, e.g., it can comprise a sampler and a skimmer cone, or a sampler cone, a skimmer cone and at least one additional cone.

The passage used for introducing the substance or mixture may, e.g., be such as described in U.S. Pat. No. 7,329,863 B2 and U.S. Pat. No. 7,119,330 B2. In the context of the present disclosure full reference is made to both references. The passages in the references given, however are used for an entirely different purpose, which is attenuating interferences. The same set-up can however also be used to facilitate molecular analysis by means of an ICP-MS, as suggested by the present disclosure.

The present disclosure advantageously allows to analyze analyte samples, in particular a molecular sample, by means of an ICP-MS utilizing an entrance-based collision/reaction cell. The analyte sample is supplied via the at least one passage such that an ion beam is formed in the reaction zone which proceeds towards the mass analyzer.

In case of a conventional ICP-MS, the plasma into which the analyte sample is introduced, generally has a relatively high pressure (e.g., atmospheric pressure). The plasma vaporizes and ionizes the sample, and the ions are subsequently extracted and transferred to a mass analyzer via a differentially-pumped interface, the mass analyzer generally operated at a relatively low pressure, typically at $<10^{-5}$ Torr. The space between succeeding cones decreases in a stepwise manner. By introducing the analyte sample into the passage instead of directly providing it to the area where the plasma is produced, an ionization process of the analyte sample becomes possible which is much softer and does not lead to a, especially complete, decomposition of the molecules, compared to the standard procedures used in ICP-MS. The disclosed procedure further enables parallel ionization of polar and nonpolar analytes, as well as ionization of gaseous and liquid analytes and also for fragmentation of molecules on purpose.

In one embodiment of the present disclosure, at least one reagent substance is added which serves for producing specific ions of the analyte sample by chemical ionization. The reagent substance may, e.g., be added via the at least one passage.

Advantageously, the reagent substance is one of H_2, O_2, H_2O, NH_3, NO_3 or any ionized, protonated or deprotonated derivative therefrom.

Another embodiment comprises that a microwave induced plasma source is used as plasma ion source. Using an ion source which includes a microwave generator has the advantage that high field strengths can be achieved along with low power dissipation. A uniform and energy efficient plasma can thus be achieved in a straightforward manner. In this regard reference is made to DE 202020106423 U1 U.S. Pat. No. 2016/0026747 A1 and WO 2017/176131 A1. In

particular, such microwave based plasma ion source may comprise a dielectric resonator.

It is of advantage if argon, nitrogen, krypton, xenon, neon, helium or any mixture of at least two gases is used as a carrier gas for the plasma ion source. The choice of carrier gas depends on the reactions that are to be induced. In this regard, nitrogen particularly leads to additional reactions with reagent gases or molecules, it can be used as a carrier gas and for ionization.

One embodiment comprises that the analyte sample is split into at least two sub-parts based on at least one physical and/or chemical property of its components, e.g., size or electrical charge, before being supplied into reaction zone via the passage, wherein the sub-parts are separately supplied into the reaction zone one after the other. Such splitting can advantageously be achieved by various separation and/or fractionation methods, such as gas or liquid chromatography or, e.g., capillary, electrophoresis. For this purpose, the mass spectrometry apparatus can include appropriate means for separating, splitting or fractionation of an analyte sample, e.g., a gas or liquid chromatography or electrophoresis unit.

A further embodiment comprises that the mass spectrometer is provided with an ion optical system establishing a reflecting electrostatic field for reflecting ions along a desired path towards the mass analyzer. Such ion optical system may include any arrangement capable of deflecting a quantity of ions between two non-parallel planes, e.g., ion mirrors, reflectors, deflectors, quadrupole ion deflectors, electrostatic energy analyzers, magnetic ion optics, ion multiple guides, and the like. One preferred embodiment employs an arrangement of an ion optics "IonMirror" devices, as described in U.S. Pat. No. 6,614,021 (incorporated herein by reference), or those disclosed in U.S. Pat. Nos. 5,559,337, 5,773,823, 5,804,821, 6,031,579, 6,815, 667, 6,630,665, or 6,6306,651. Using an ion mirror further increases the sensitivity of the ICP-MS device.

In another embodiment of the method, the interface structure:

separates a first vacuum region at a relatively high pressure adjacent a first surface of said interface structure, which receives the plasma flux from the plasma ion source from a second vacuum region at a relatively low pressure adjacent a second surface of said interface structure, which leads to the mass analyzer; and

provides an aperture having axial extension forming the reaction zone located between the first surface and the second surface of the interface structure, through which the plasma flux flows from the first region towards the second region, and wherein the passage leads into the reaction zone formed in the aperture of the interface structure.

The analyte sample thus is directed into the reaction zone where it interacts with the plasma which is already at a lower pressure compared to the pressure in the area of the plasma ion source. This makes the ionization much softer and leads to notably less fragmentation processes.

One embodiment comprises that the interface arrangement at least comprises a sampling cone and a skimmer cone, the skimmer cone being arranged behind the sampling cone.

Yet, in another embodiment, at least two passages are provided in the interface arrangement. The at least two passages may be provided in the same cone or in two different cones, e.g., one in the skimmer cone and one in the sampling cone. By providing more than one passage, more than one reaction zone is created enabling for multi-reactions.

In one embodiment, the passage is completely located within at least one cone, e.g., the sampler, the skimmer cone or any other cone. Such device is, e.g., suggested in U.S. Pat. No. 7,329,863 B2.

In another embodiment however, the passage is located behind the sampler cone, the skimmer cone or any other cone, as described in U.S. Pat. No. 7,119,330 B2.

In a further embodiment the analyte sample and/or the reagent substance is/are supplied via the passage at least during a first time interval and supplied to an area of the plasma ion source, where the plasma is formed, at least during a second time interval. By this procedure, a conventional ICP-MS analysis relating to a structural analysis can be combined with a molecular analysis. The first and second time interval can be carried out alternately, or can be initiated on demand.

The object of the present disclosure is further achieved by use of an inductively coupled mass spectrometry apparatus, the mass spectrometry apparatus including a plasma ion source, a mass analyzer and an interface arrangement positioned between the plasma ion source and the mass analyzer of the mass spectrometer, the interface arrangement at least comprising an interface structure in the form of a cone of the interface arrangement, e.g., a sampling cone or a skimmer cone, and at least one passage with an inlet and an outlet, the passage leading from an outside of the interface structure into a reaction zone formed in an area surrounding the outlet of the passage, for analyzing a molecular analyte sample. The mass spectrometry apparatus is in particular used for molecular analysis by carrying out a method according to at least one of the embodiments described above.

BRIEF DESCRIPTION OF THE DRAWINGS

The present disclosure as well as its preferred embodiments will be further explained based on the figures, which include:

FIG. **1** shows a conventional ICP-MS according to the state of the art;

FIGS. **2***a*-**2***d* show exemplary embodiments for an interface arrangement with at least one cone having at least one passage for introducing the analyte sample; and

FIG. **3** shows a mass spectrum of propane obtained with a method according to the present disclosure.

In the figures, same elements are provided with the same reference numbers.

DETAILED DESCRIPTION

FIG. **1** schematically illustrates a conventional ICP-MS **10** with an ion source **20** in the form of an inductively coupled plasma torch having a central tube for conveying the analyte sample AS in a carrier gas into a plasma **28** produced in the torch. The ion source **20** further includes an intermediate tube for conveying a plasma forming gas **24** and an auxiliary gas **26**, which can, e.g., be argon or nitrogen, a radio frequency coil **30** arranged around the outer tube.

The mass spectrometer further comprises an interface arrangement **32** for transferring the analyte sample and plasma flux **28** into the analyzing part of the ICP-MS including an interface structure comprising a sampling cone **34** and a skimmer cone **40**. Both cones **34**, **40** each have a hole **36**, **42** at its apex through which the plasma flux **28**

passes from the ion source **20** into a fist **38** and second **44** vacuum region. The cones **34**, **40** are typically water-cooled. The second vacuum region **44** in the embodiment shown further comprises an ion extraction electrode **46** and other ion optics [not shown] all being part of the ion optical system, which serves for extracting an ion beam from the plasma flux **28** into a third pumped vacuum region **48** and towards mass analyzer **50** which separates the ions according to their mass-to-charge-ratio and towards detector **52**, where the detected ions are read out by recording means **54**. Different mass analyzers **50**, such as a quadrupole or time-of-flight (TOF) mass analyzer **50** may be employed. Utilizing a TOF analyzer has the advantage of being capable of discriminating resulting polyatomic ions.

The interface arrangement **32** used for carrying out the method according to the present disclosure comprises at least one passage with an inlet and an outlet, the passage leading from an outside of the interface structure into a reaction zone formed in an area surrounding the outlet of the passage as illustrated in FIGS. **2***a*-**2***c*, which show exemplary embodiments for an interface arrangement **32** with at least one passage in at least one cone.

The interface arrangement **32** shown in FIG. **2***a* has a sampling cone **34** and a skimmer cone **40** similar to that shown in FIG. **1**. The ion plasma flux **28** flows through hole **36** in sampling cone **34** into the first vacuum region **38** and through hole **42** into the second vacuum region **44** held at a pressure lower than that of the first vacuum region. The skimmer cone **40** includes a passage **60** leading from an inlet **62** to an outlet **63** at the hole **42** of the skimmer cone **40**. While such arrangement conventionally was used to create a reaction/collision zone, the present disclosure uses the passage **60** to supply the analyte substance AS into the reaction zone **64** where it interacts with the plasma **28** thereby softly ionizing the analyte substance AS. The exact dimensions of the reaction zone **64** depend on several factors, e.g., properties of the plasma. The shape of the reaction zone in FIG. **2***a* is thus only exemplarily and can vary from device to device.

A second preferred embodiment of the interface arrangement **32** is shown in FIG. **2***b*. In contrast to the embodiment shown in FIG. **2***a*, in case of FIG. **2***b* the sampling cone **34** comprises a second passage **74** with inlet **72** and outlet **75** creating a second reaction zone **76** in proximity to hole **36**. The two passages **60** and **74** can be used in different ways. As indicated in FIG. **2***a*, a reagent gas RG may be supplied via passage **72** while the analyte sample AS is supplied via passage **60**. However, in other embodiments, e.g., the reagent substance RS may also provide via passage **60** while the analyte sample AS is supplied via passage **74**. One single passage **60**, **74** can also be used for supplying both reagent substance RS and analyte sample AS.

A third preferred embodiment for an interface arrangement **32** is shown in FIG. **2***c*. In contrast to the embodiment shown in FIG. **2***b*, the skimmer cone **40** is provided with two passages **60** and **88**. The third passage **88** also has an inlet **90** and an outlet **91**, which in the present embodiment leads into the first reaction zone **64**. Again, many different possibilities exist for using the different passages **60**, **74**, **88**, and for supplying one or more reagent substances RS and analyte samples AS which all fall under the scope of the present disclosure.

Finally, another preferred embodiment of the interface arrangement **32** is subject to FIG. **2***c*. Again, the interface arrangement **32** includes a sampler cone **34** and a skimmer cone **40** followed by an ion optical system including an ion extraction electrode **45** mounted on the skimmer cone **40** by a dielectric seal **45***a* and other electrodes **46** and **47** to extract ion beam **58**. For this embodiment, the at least one passage **94** is provided behind the skimmer cone **40** for supplying the analyte sample AS into reaction zone **95**.

It shall be noted that the different embodiments for the interface arrangement **32** shown can arbitrarily combined with each other. Further, it shall be noted that the present disclosure is by no means limited to the embodiments shown. For instance, any embodiment for an interface arrangement **32** or interface structure **32**, **40** e.g., as disclosed in U.S. Pat. No. 7,329,863 B2 and U.S. Pat. No. 7,119,330 B2.

In summary, the present disclosure provides for a possibility to combine conventional ICP-MS for elemental analysis with organic analysis of molecules in one single device. To achieve this, passages **60**, **74**, **88**, **94** conventionally provided for reducing interferences by supplying collision gases, now and for the first time, are used to supply the analyte sample AS into the mass spectrometry device. The analyte sample AS, in particular a molecular sample, are either ionized by the incoming already cooled down plasma, the residual plasma, or by a carrier gas, e.g., stemming from the ion source **20**.

It is furthermore possible to add additional reagent substances RD via the at least one passage **60**, **74**, **88**, **94** to produce specific product ions by chemical ionization, that can be analyzed by the subsequent mass spectrometry analyzing section.

FIG. **3** shows two mass spectra of propane, mass spectrum **1** obtained with a conventional ICP mass spectrometer apparatus **10**, and mass spectrum **2** obtained with a method and device **10** according to the present disclosure, i.e. the analyte sample AS is introduced via a passage **60**, **74**, **88**, **94** of interface arrangement **32**, using an entrance-based collision/reaction cell. By introducing the analyte sample AS into the passage **60**, **74**, **88**, **94** instead of directly providing it to the area where the plasma is produced, the ionization process of the analyte sample AS becomes much softer and does not lead to a decomposition of the molecules (spectrum **2**), compared to the standard procedures used in ICP-MS (spectrum **1**). Only in spectrum **2** the propane molecules of the analyte sample AS shown in FIG. **3** remain intact (44 Da) or partially fragmented (e.g., 43 Da—corresponding to a loss of one hydrogen, 26-30 DA—corresponding to various C_2H_n fragments). The present disclosure therefore expands the scope of application of ICP-MS devices towards molecular analysis in a straightforward manner.

We claim:

1. A method of operating an inductively coupled plasma mass spectrometry apparatus for analyzing an analyte sample, wherein the mass spectrometry apparatus comprises:

a plasma ion source;

a mass analyzer; and

an interface arrangement disposed between the plasma ion source and the mass analyzer, the interface arrangement comprising an interface structure including at least one cone and a passage having an inlet and an outlet, wherein the passage extends from an exterior of the interface structure into a reaction zone defined in an area surrounding the outlet of the passage,

the method comprising:

generating a plasma using the plasma ion source and forming a plasma flux to flow towards the mass analyzer;

supplying the analyte sample into the reaction zone via the passage such that the analyte sample interacts with the plasma flux; and

analyzing the analyte sample using the mass analyzer.

2. The method of claim **1**, wherein at least one reagent substance is added which is selected to generate specific ions of the analyte sample by chemical ionization.

3. The method of claim **2**, wherein the at least one reagent substance is one of H2, O2, H2O, NH3, NO3 or any ionized, protonated or deprotonated derivative thereof.

4. The method of claim **2**, wherein the analyte sample and/or the reagent substance is/are supplied via the passage at least during a first time interval, and

wherein the analyte sample and/or the reagent substance is/are supplied into an area of the plasma ion source at least during a second time interval.

5. The method of claim **1**, wherein the plasma ion source is a microwave induced plasma source.

6. The method according to claim **5**, wherein argon, nitrogen, krypton, xenon, neon, helium or any mixture of at least two gases is a carrier gas for the plasma ion source.

7. The method of claim **1**, wherein the analyte sample is split into at least two sub-parts based on at least one physical and/or chemical property of components of the analyte sample before being supplied into reaction zone via the passage, and wherein the at least two sub-parts are separately and serially supplied into the reaction zone.

8. The method of claim **1**, wherein the mass spectrometry apparatus further comprises an ion optical system configured to establish a reflecting electrostatic field adapted to reflect ions along a desired path towards the mass analyzer.

9. The method of claim **1**, wherein the interface structure is configured as to:

separate a first vacuum region at a relatively high pressure adjacent a first surface of the interface structure, which receives the plasma flux from the plasma ion source from a second vacuum region at a relatively low pressure adjacent a second surface of the interface structure, which is connected to the mass analyzer; and

define an aperture having axial extension defining the reaction zone located between the first surface and the second surface of the interface structure, through which the plasma flux flows from the first region towards the second region, and

wherein the passage connects into the reaction zone in the aperture of the interface structure.

10. The method of claim **1**, wherein the at least one cone of the interface arrangement includes a sampling cone or a skimmer cone.

11. The method of claim **1**, wherein the at least one cone of the interface arrangement includes a sampling cone and a skimmer cone, the skimmer cone disposed behind of the sampling cone.

12. The method of claim **11**, wherein the passage is located behind of the sampler cone, the skimmer cone and/or an additional cone.

13. The method of claim **1**, wherein the passage is completely located within the at least one cone.

14. The method of claim **1**, wherein the interface arrangement includes at least two passages.

15. A method of molecular analysis of a molecular analyte sample, the method comprising:

providing an inductively coupled plasma mass spectrometry apparatus, comprising:

a plasma ion source;

a mass analyzer; and

an interface arrangement disposed between the plasma ion source and the mass analyzer, the interface arrangement comprising an interface structure including at least one cone and a passage having an inlet and an outlet, wherein the passage extends from an exterior of the interface structure into a reaction zone defined in an area surrounding the outlet of the passage; and

performing a molecular analysis of the molecular analyte sample using the mass spectrometry apparatus.

* * * * *